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199 31 413.6	8 July 1999 (08.07.1999)	DE
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199 32 209.0	9 July 1999 (09.07.1999)	DE
199 32 914.1	14 July 1999 (14.07.1999)	DE
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/00804 A3

(54) Title: *CORYNEBACTERIUM GLUTAMICUM* GENES ENCODING STRESS, RESISTANCE AND TOLERANCE PROTEINS

(57) Abstract: Isolated nucleic acid molecules, designated SRT nucleic acid molecules, which encode novel SRT proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing SRT nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated SRT proteins, mutated SRT proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of SRT genes in this organism.

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/31 C12N1/21 C12Q1/68 C07K14/34

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EBI [Online] AC X13385, 19 March 1999 (1999-03-19) BARASH S. ET AL.: "Enterococcus faecalis genome contig" XP002152527 abstract --- JAEGER WOLFGANG ET AL: "A Corynebacterium glutamicum gene conferring multidrug resistance in the heterologous host Escherichia coli." JOURNAL OF BACTERIOLOGY, vol. 179, no. 7, 1997, pages 2449-2451, XP002152524 ISSN: 0021-9193 the whole document --- -/--	6,8
X		1,2, 8-19,22

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 November 2000	13. 02. 01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kania, T

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WEHRMANN AXEL ET AL: "Different modes of diaminopimelate synthesis and their role in cell wall integrity: A study with Corynebacterium glutamicum." JOURNAL OF BACTERIOLOGY, vol. 180, no. 12, June 1998 (1998-06), pages 3159-3165, XP002152525 ISSN: 0021-9193 cited in the application the whole document	1,2,8, 19,22
X	PETER H ET AL: "CORYNEBACTERIUM GLUTAMICUM IS EQUIPPED WITH FOUR SECONDARY CARRIERSFOR COMPATIBLE SOLUTES: IDENTIFICATION, SEQUENCING, AND CHARACTERIZATION OF THE PROLINE/ECTOINE UPTAKE SYSTEM, PROP, AND THE ECTOINE/PROLINE/GLYCINE BETAINE CARRIER, ECTP" JOURNAL OF BACTERIOLOGY,WASHINGTON, DC,US, vol. 180, no. 22, 1998, pages 6005-6012, XP000917352 ISSN: 0021-9193 the whole document	1,2, 8-19,22
X	CHAN MING-SHUN ET AL: "Cloning of m-fluorophenylalanine-resistant gene and mutational analysis of feedback-resistant prephenate dehydratase from Corynebacterium glutamicum." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 219, no. 2, 1996, pages 537-542, XP002152526 ISSN: 0006-291X the whole document	1,2, 8-19,22
X	EP 0 752 472 A (AJINOMOTO KK) 8 January 1997 (1997-01-08) the whole document	1,2, 8-19,22, 25-34
X	WO 99 02692 A (YAGOSHI CHIZU ;AJINOMOTO KK JP); KIMURA EIICHIRO (JP); NAKAMURA J) 21 January 1999 (1999-01-21) the whole document & EP 1 002 866 A (AJINOMOTO KK) 24 May 2000 (2000-05-24)	1,2, 8-19,22, 25-34
X	WO 88 09819 A (MASSACHUSETTS INST TECHNOLOGY) 15 December 1988 (1988-12-15) the whole document	1,2, 8-19,22, 25-34

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR 2 607 827 A (PASTEUR INSTITUT) 10 June 1988 (1988-06-10) the whole document ---	1-38
A	EP 0 252 558 A (SCLAVO SPA) 13 January 1988 (1988-01-13) the whole document ---	35
P,X	DATABASE EBI [Online] AC AF237667, 14 March 2000 (2000-03-14) KIM H. AND LEE H.: "Nucleotide sequence of the lmrB gene in Corynebacterium glutamicum" XP002152528 abstract -----	1-24

INTERNATIONAL SEARCH REPORT

ıational application No.
PCT/IB 00/00922

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-38 partially

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: invention 1: claims 1-38 partially

An isolated nucleic acid molecule from Corynebacterium glutamicum encoding a stress, resistance, or tolerance gene disclaiming the F-designated genes in table 1. Said gene having the SEQ ID NO:1, homologs (at least 50% homology), variants, and DNA sequences hybridizing thereto, as well as vectors and host cells comprising said sequences. An isolated stress, resistance, or tolerance polypeptide from C. glutamicum. Said protein having the SEQ ID NO:2, homologs (at least 50% homology), and variants thereof. The use of said sequences to modify the production of or produce a fine chemical from said host cell, the fine chemical especially being an amino acid.A method for diagnosing the presence or activity of Corynebacterium diphtheriae in a subject employing said sequences.A host cell comprising said nucleic acid sequences wherein said sequences are disrupted modified, or under the control of a heterologous regulatory region.

2. Claims: inventions 2-122: claims 1-38 partially

as invention 1 but relating to the pairs of sequences as listed in Table 1 (apart from the ones disclaimed)

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